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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,794	08/21/2003	Andrew J. Bett	20699Y	8205

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EXAMINER	
BROWN, TIMOTHY M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,794	BETT ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *12-20 and 24-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/04 et seq*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received August 21, 2003, and the telephonic interview of December 9, 2005. Claims 1-11 and 21-23 are under examination. Claims 12-20 and 24-83 are withdrawn.

Interview

The Examiner issued a telephonic restriction during a telephonic interview with Anna Cocuzzo on December 9, 2005. Ms. Cocuzzo kindly elected to prosecute, without traverse, the invention defined by Group I, species i and iv. The restriction requirement as issued appears below.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, 21-23, 30, 45, 58 and 73, drawn to a means for propagating replication defective adenovirus in an adenoviral-complementing cell line expressing E1 gene products which are non-native to the adenovirus, classified in class 435, subclass 235.1.

II. Claims 12-20, 24-29, 31-35, 38, 40-44, 46-48, 51, 53-57, 59-63, 66, 68-72, 74-76, 79, and 81-83, drawn to a replication-defective adenovirus comprising all or a portion of a heterologous E4 region or portion thereof, classified in class 435, subclass 235.1.

III. Claims 36, 37, 39, 49, 50, 52, 64, 65, 67, 77, 78 and 80, drawn to a method for administering a heterologous nucleic acid to a subject, classified in class in class 435, subclass 235.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). Here, the heterologous adenovirus of Invention I can be made by transforming an pIX helper cell line with a heterologous replication-defective adenovirus. Thus, the product of Invention II can be made by a materially different process.

Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions have different functions as Invention I is drawn to propagating replication-defective adenovirus, while Invention III is a method for administering a heterologous nucleic acid. Inventions I and III also have different modes of operation. Invention I introduces a heterologous nucleic acid to a replication-defective adenovirus. Invention III, in contrast, admininisters a nucleic acid to a subject. Accordingly, Inventions I and III are unrelated due to their different functions and different modes of operation.

Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, Invention II comprises a heterologous adenovirus and cell line

transformed with said adenovirus. This heterologous adenovirus can be used in an antiviral assay, while the adenovirus-transformed cell line may be used to determine the cytoxicity of a compound. Accordingly, Inventions II and III may be restricted as product and process of use.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

An election of any one of Inventions I-III requires a further election of one of the following combinations of heterologous adenovirus serotype:

i. Adenvirus serotypes 5 and 35

ii. Adenvirus serotypes 24 and 56

iii. Adenvirus serotypes 34 and 5

An election of any one of Inventions I-III requires a further election of one of the following HIV antigens:

iv. gag

v. pol

vi. nef

vii. env

Species i-iii are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Here, the specification does

not disclose a method wherein heterologous adenoviruses of different serotype combinations can be used together. Moreover, Species i-iii have different effects due to their distinct chemical compositions and distinct immunogenicities. Thus, Species i-iii are therefore unrelated.

Species iv-vii are also unrelated. The specification does not disclose a specific method wherein a combination of the listed HIV antigens are used with one another. Moreover, these antigens have different amino acid compositions and therefore different biological activities. Thus, Species iv-vii are unrelated.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the

examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

Claim 1 is objected to for being ungrammatical. Amending the claim to recite "a heterologous E4 region comprising a nucleic acid . . ." would overcome this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 21-23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation of "wherein the E4 region or portion thereof inserted into the adenovirus is native to a virus of the same adenovirus serotype as the E1 gene product . . . ." It is unclear whether "native to a virus of the same serotype as the E1 gene" requires that the E4 region and the E1 gene product to be from the same serotype. Amending the claim as follows would overcome this rejection: "wherein the E4 region or portion thereof is of the same adenovirus serotype as the E1 gene product . . . ."

Claim 7 is indefinite in that "the subgroup C adenovirus" lacks antecedent basis.

Claims 4 and 5 are indefinite for lacking antecedent basis for "the replication-defective virus." Amending the claims to recite "the replication-defective adenovirus . . ." would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 7, 10 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ji et al. (Ji, L. Reduced toxicity, attenuated immunogenicityt and efficient mediation of human p53 gene expression in vivo by an adenvirus vector with deleted E1-E3 and inactivated E4 by Gal4-TATA promoter replacement" *Gene Therapy* (1999) 6; 393-402).

Applicants claim a means for propagating replication-defective adenovirus comprising inserting a heterologous E4 region comprising ORF6 into a replication- defective serotype 5 adenovirus, introducing the replication defective adenovirus comprising said heterologous E4 insert to an E1-complimenting cell line, and rescuing the replication-defective adenovirus. The heterologous replication-defective adenovirus may comprise a gene of interest.

Ji et al. disclose propagating a recombinant adenovirus in an E1-complementing cell line wherein the adenovirus comprises deletions in E1, E3 and E4, and a heterologous promoter

operatively connected to the E4 region. Based on this disclosure, Ji et al. anticipate the subject matter of claims 1, 6, 7, 10 and 21.

Claims 1-7 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Mehtali et al. (US 6,475,480 B1).

Applicants claim a means for propagating replication-defective adenovirus comprising inserting a heterologous E4 region comprising ORF6 into a replication- defective serotype 5 adenovirus, introducing the replication defective adenovirus comprising said heterologous E4 insert to an E1-complimenting cell line, and rescuing the replication-defective adenovirus. The heterologous E4 region may comprise the entire E4-encoding region and native E4 promoter. The heterologous E4 region may be substituted in place of the entire E4 promoter of the replication-defective adenovirus.

Mehtali et al. disclose a method of propagating replication-defective adenovirus comprising inserting a heterologous E4 region into an E1 deficient serotype 5 adenovirus, introducing the replication-defective adenovirus comprising the heterologous E5 insert into an E1-complementing cell line, and rescuing propagated replication-defective adenovirus (col. 2, lines 56-59, 65-67; col. 3, lines 1-15, 37-40, 65-67; col. 4, lines 1, 35-41, 44-46; and col. 7, lines 54-67). Based on this disclosure, Mehtali et al. anticipate the subject matter of claims 1-7 and 10.

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehtali et al. (US 6,475,480 B1) in view of Inglis et al. (US 5,665,362).

Mehtali et al. teach all the limitations discussed above. Mehtali et al. do not expressly teach a heterologous gene of interest comprising HIV-1 gag. However, Inglis et al. disclose producing a replication-defective adenovirus comprising a nucleotide encoding an HIV-1 gag antigen (col. 2, lines 5-11, 30-31; col. 5, lines 56-67). Mehtali et al. expressly provide that HIV antigenic polypeptides can be inserted into their replication-defective adenovirus as a means for providing anti-HIV therapy (col. 6, lines 41-44). Therefore, it would have been obvious to one skilled in the art to insert a gag peptide in a replication-defective adenovirus vector as claimed by Applicants.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

i. Vogels et al. WO 03/104467 A1 (18 December 2003) Means and methods for the production of adenovirus vectors

ii. Vogels et al. WO 2004/001032 A2 (31 December 2003) Stable adenoviral vectors and methods for propagation thereof

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

JAMES HOUSEL 1/9/06
SUPERVISORY PATENT EXAMINER
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TMB 12/29/05